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Center for Biologics Evaluation and Research
Open Public Forum
14 August 1998

Comments on Implementation of FD&C Act
as amended by FDAMA

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Background

Massachusetts Biotechnology Council

- Representing ~ 200 companies
  - Mostly Small to Medium Size
  - Early stage development to commercialized products
- 13 year history of ensuring that "Biotech" Companies reach full potential

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FDAMA Implementation Process Review

- MBC supports the FDA in its FDAMA mission to realize the "prompt approval of safe and effective new drugs and other therapies ... so that patients may enjoy the benefits provided by these therapies to treat - and prevent illness and disease"

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FDA Modernization Objectives

(1) Maximize availability and clarity of information about application and submission review process,

(2) Maximize the availability and clarity of information for consumers and patients concerning new products,

(3) Implement inspection and postmarket monitoring provisions,

(4) Assure access to the scientific and technical expertise needed to carry out FDA's obligations,

(5) Establish mechanisms for meeting specified time periods for the review of applications and submissions, and

(6) Eliminate backlogs in the review of applications and submissions.

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FDAMA Implementation Process Review

MBC Working Groups Formed to

- Collectively Identify Concerns with FDA Review Process
- Propose Improvements during FDAMA Implementation

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FDAMA Implementation Process Review

Specific Priority Issue Areas Addressed

(1) Performance Goals, User Fees & Meetings
(2) Manufacturing Changes
(3) Fast Track
(4) Off-Label Uses
(5) Pharmacoeconomics

Common Concerns Of Member Companies

(A) Harmonization and Consistency
(B) Increased Transparency
(C) Enhancement of Role of Ombudsman / Cooperation between FDA & Industry

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FDAMA Implementation Process Review

Result - MBC "White Paper"

Food and Drug Administration Modernization Act of 1997

Recommendations for Implementation and Regulation

(Submitted to FDA on 18 July 1998)

- Proposed "Points to Consider" Documents
- Recommendations for Common Concerns

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FDAMA Implementation Process Review

Proposed "Points to Consider" Documents

§119:	Meetings & Performance Goals
§116:	Manufacturing Changes
§112:	Fast Track
§401:	Off-Label Use
§114:	Health Care Economic Information

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Proposed Points to Consider

§119: Meetings & Performance Goals

- **Key Objective**

  Delivery of breakthrough products to patients in time-sensitive manner

  - **Establish agreements on the design of clinical trials and preclinical studies,**
  - **Resolve any issues in a timely manner, and**
  - **Maintain consistency in review process**

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Proposed Policy Committee

§119: Meetings & Performance Goals

- **Proposed Guidance**

  Defined Obligations of Sponsor & Agency regarding

  - » **Setting Up Meetings**
  - » **Holding Meetings**
  - » **Meeting Minutes**
  - » **Types of Meetings**
  - » **Performance Goals**

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Proposed Policy Committee

§116: Manufacturing Changes

- **Key Objectives**
  - **Clarification of Major / Minor Changes**
    - » **Uniformity of Change Classifications**
  - **Guidance Document (Not Regulation)**

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Proposed Policy Committee

§116: Manufacturing Changes

- **Proposed Guidance**
  - **Reporting Changes based upon potential to effect identity, quality, strength, purity, or potency**
    - » **Substantial:** Preapproval
    - » **Moderate:** Supplement with Notice
    - » **Minimal:** Notice in Annual Report
  - **Comparability Protocols**
  - **Labeling Changes**

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Proposed Points of Emphasis

§112: Fast Track Drugs & Biologics

- **Key Objective**

  Provide appropriate FDA priority to potential therapeutic breakthrough products

  - Clarification of Definitions
    - » Serious & Life Threatening Conditions
    - » Unmet Medical Need
  - Clarification of Designation and Review Process

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Proposed Points of Emphasis

§112: Fast Track Drugs & Biologics

- Proposed Guidance
  - Apply PUDFA-2 Performance Goals - First to Fast Track
    - » Serious and Life Threatening Condition
    - » Demonstrated Potential to Address Unmet Medical Needs
    - » Surrogate Endpoints
      - Guidance document should also discuss:
        - Selection of surrogate endpoints
        - Use of professional societies, etc.
        - Quality of life scales as primary clinical endpoints
        - Dissemination of information of surrogate endpoints
  - Designation by Directors of Review Divisions
  - Highly Interactive IND Process with Action Dates
  - Rolling Review of BLA submissions

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Proposed Points of Emphasis

§112: Fast Track Drugs & Biologics

- Proposed Guidance (Continued)
  - Alternative Standard for Marketing (Surrogate Endpoint)
    - » Subsection (b(2))

      "Reasonably like to predict clinical Benefit"
      - Congressional intent to apply to unvalidated data regardless of whether surrogate or clinical endpoint
      - Consider limitations of alternative therapies
        - Is safety and efficacy sufficient?
        - FDA Subpart E regulation: 90% chance of effectiveness better than none at all
  - Postapproval Requirements
    - » FDA may (not mandated) require Phase IV studies and/or preapproval of marketing literature
      - Preapproval of promotional material - Terminate 6 months after product approval

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Proposed Points to Convey

§401: Off-Label Use Information

- **Key Objective**

  Provide Health Care Professionals with the best information available to treat patients and to make health care decisions

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Proposed Points to Convey

§401: Off-Label Use Information

- **Proposed Guidance**
  - **Comments on FDA Proposed Rule (FR - June 8, 1998) submitted on July 23, 1998**
    - **Criteria for acceptable journal articles and reference texts is too restrictive**
    - **Mandatory disclosures**
      - **Level of detail required**
      - **Manner of display**
    - **Economically prohibitive exemption ineffective**
    - **Narrow definition of "unapproved uses"**
    - **Internet reporting**
  - **Support of PhRMA's Comments on Proposed Rule**

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Proposed Points to Convey

§114: Health Care Economic Information

- **Key Objective**

  Provide Economic Data to support
  - **Managed Care Organizations,**
  - **Integrated Delivery Systems, and**
  - **Other Organizations' Drug Selection Decisions**

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Proposed Points to Consider

§114: Health Care Economic Information

- **Key Issues**
  - Competent and reliable scientific evidence standard
  - Limitations on scope of Section 114
    - Directly related to an approved indication
    - Permitted audience
  - Health Care Economic Information
    - Definition - All Forms intended to facilitate decision making
      - Cost Analyses
      - Cost Effective Analyses
      - Cost Benefit Analyses
    - Mfg's can use reasonable assumptions of the HCE consequences derived from the approved indication

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Proposed Points to Consider

§114: Health Care Economic Information

- **Key Issues (continued)**
  - Health Care Economic Information (continued)
    - Clinical outcomes may include physiologic, anatomic and biologic endpoints, health status and quality of life measures, quality adjusted life expectancy, measures of patient performance or satisfaction or other measures relevant to decision makers
    - Can disseminate information in many ways, but must report to FDA upon first use
    - FDA use experts to evaluate substantiation
  - Support of PhRMA's "Guidance for Industry: Promotional Use of Health Care Economic Information"

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FDAMA Implementation Process Review

Recommendations for Common Concerns

(A) Harmonization and Consistency in the Handling of Drugs and Biologics

(B) Increased Transparency and Accountability

(C) Cooperation between the FDA & Industry and Enhancement of the Roles of Industry Ombudsmen

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Recommendations of Common Concern

Harmonization and Consistency in the Handling of Drugs and Biologics

- Discussion Points
  - Promotion of Science - CBER as model
  - Uniform Personnel Training
    - Consistent response to FDAMA-related changes
  - Subset Analysis
    - Age, Gender and Race
    - Uniformity & Consistency in acceptance
    - Adoption of Feb. 11, 1998 - Final Rule, IND and NDA, 63 Fed. Reg. 6854-6852
  - Transparency

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Recommendations of Common Concern

Increased Transparency and Accountability

- Discussion Points
  - Disclosure of Draft Submission Documents
    - Review by sponsors prior to submission to Advisory Panels
      - Allows preparation of responsive documents
      - Allows clarification
      - Allows improved accuracy of contents
  - Additional Proposals
    - Self-Reviewing / Self-Policing Mechanisms
      - Uniform timetables
      - Regular publication of performance results
      - Expansion of Ombudsman role

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Recommendations of Common Concern

Cooperation between the FDA & Industry and Enhancement of the Roles of Industry Ombudsmen

- Discussion Points
  - Industry Input
  - Enhance Role of Ombudsman
    - Agency wide jurisdiction vs center level
    - Proactive issue forums
  - Revision in Complaint Review Procedure
    - New open filing of issues about reviewers, policy challenges for Agency & public scrutiny

MBC Summary

Request for FDA Action

- Review of proposed Points to Consider and recommendations regarding common concerns
- Utilize MBC Working Groups as Resource to respond to specific queries and provide industry perspective
- In spirit of FDAMA, join in ongoing dialogue to address concerns